IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Attorney Docket No. 01-1081)

In the Application of:	
Graf et al.	**Examiner: Ford, Vanessa L.**
Application No.: 09/937,103	**Group Art Unit: 1645**
Filing Date: July 5, 2002	**Confirmation No.: 4719**
For: Use of Trehalose For Stabilizing A Liquid Vaccine	

RESPONSE TO THE OFFICE ACTION MAILED DECEMBER 12, 2003

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In response to the office action mailed December 12, 2003, please amend the above-identified application as follows and consider the following remarks.

Amendments to the Written Description begin on page 2 of this paper.

Amendments to the Claims are reflected in the listing of claims that begins on page 5 of this paper.

Remarks begin on page 7 of this paper.

CERTIFICATE OF FACSIMILE (37 C.F.R. 1.8)

The undersigned hereby certifies that this Transmittal Letter and the paper, as described in paragraph 1, are being transmitted via facsimile (703) 872-9306 to the Commissioner For Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on March 12, 2004.

Date: March 12, 2004

Michael S. Greenfield

Amendments to the Written Description:

Please replace the paragraph at page 1, lines 8-35 with the following amended paragraph:

Such vaccine compositions, some of whose antigens have to be bound to carrier proteins in order to be immunogenic, are known in the prior art. This is in particular the case for compositions intended for vaccination against infections caused by the bacterium ~~Haemophilus influenzae~~ *Haemophilus influenzae* type b, which comprise, as vaccine antigen, the capsular polysaccharide of the bacterium or Polyribosylribitol Phosphate (PRP) coupled to the tetanus toxoid T. Such vaccine compositions tend to lose their immunogenicity, and therefore their efficacy, over time. To overcome this drawback, the solution generally proposed in the prior art is freeze-drying. This solution, which is satisfactory from the point of view of the result obtained as regards preservation of immunogenicity, has, nevertheless, the disadvantage of making the method of manufacture cumbersome, and therefore of increasing the cost thereof. In addition, at the time of administration of the vaccine, it is necessary to carry out an additional operation of taking up the freeze-dried product in a sterile liquid, which, on the one hand, represents an additional constraint for the practitioner and, on the other hand, comprises, like any manipulation, the risk of being poorly carried out. It is therefore desirable to find another solution to the problem of the loss of immunogenicity, over time, of the polysaccharide antigens bound to a carrier protein when they are present in a liquid vaccine composition.

Please replace the paragraph at page 2, line 24 to page 3, line 10 with the following amended paragraph:

The vaccine composition according to the invention may be a monovalent composition, that is to say that it is intended for protection against a single disease, or a multivalent composition, that is to say that it is intended to protect the individual to whom it has been administered, against several diseases. In all cases, at least one of the vaccine valencies is represented by a polysaccharide antigen bound to a carrier protein. Among the polysaccharide antigens capable of entering into the composition of a vaccine and of being stabilized according to the invention, there may be mentioned the polysaccharides present in the capsules of bacteria, the polysaccharides present in the walls of Gram-negative bacteria or the polysaccharides present in the walls of fungi. Thus, it is possible to use the polysaccharides encountered in the following microorganisms: ~~Pseudomonas~~ *Pseudomonas* (for example ~~P. aeruginosa~~*P. aeruginosa*), ~~Saphylococcus~~*Staphylococcus*, ~~Steptococcus~~ *Streptococcus* (for example ~~S. pneumoniae~~*S. pneumoniae*), ~~Klebsiella~~ *Klebsiella* (for example ~~K. pneumonia~~*K. pneumonia*), ~~Salmonella~~ *Salmonella* (for

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FACSIMILE TRANSMITTAL LETTER

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
Facsimile: 1-703-872-9306
Total Pages: 9

Dear Sir:

In regard to the above identified application,

1. We are transmitting herewith the attached:

   a) Response to Office Action Mailed December 12, 2003.

2. With respect to fees:

   a) A fee is not required at this time.
   b) Please charge any underpayment or credit any overpayment our Deposit Account, No. 13-2490.

3. CERTIFICATE OF FACSIMILE UNDER 37 CFR § 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described in paragraph 1, are being transmitted via facsimile (703-872-9306) to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on March 12, 2004.

Respectfully submitted,

Dated: March 12, 2004

Michael S. Greenfield
Registration No. 37,142

McDonnell Boehnen Hulbert & Berghoff
300 South Wacker Drive, 32nd Floor
Chicago, IL 60606
(312)913-0001

example ~~S. typhi~~*S. typhi* and ~~S. paratyphi~~*S. paratyphi*), ~~Escherichia coli~~*Escherichia coli*, ~~Neisseria~~ *Neisseria* (for example ~~N. meningitidis~~*N. meningitidis*), ~~Shigella~~ *Shigella* (for example ~~S. dysenteria~~*S. dysenteria*, ~~somnei~~ *somnei* or ~~flexneri~~*flexneri*), ~~Haemophilus~~ *Haemophilus* (for example ~~H. influenzae~~*H. influenzae* type b), ~~Moraxella~~*Moraxella*, ~~Vibrio cholerae~~*Vibrio cholerae*, ~~Mycobacterium tuberculosis~~*Mycobacterium tuberculosis*, ~~Candida~~*Candida*, ~~Cryptococcus neoformans~~*Cryptococcus neoformans* and ~~Hansenula~~*Hansenula*.

Please replace the paragraph at page 3, lines 12-15 with the following amended paragraph:

The present invention has shown all its benefit for vaccine compositions comprising the capsular polysaccharide of ~~Haemophilus influenzae~~*Haemophilus influenzae* type b or Polyribosylribitol Phosphate.

Please replace the paragraph at page 3, lines 17-35 with the following amended paragraph:

The polysaccharides generally used as vaccine antigens generally exhibit the characteristic of being T-independent, that is to say in particular that the memory of the immune system in relation to such antigens is weak and that these polysaccharides are generally not immunogenic in young children. To make them T-dependent, it is customary to combine them with carrier proteins (protein, for the purposes of the present invention, also includes peptides or polypeptides) in order to obtain a polysaccharide-carrier protein conjugate. These proteins are in particular those normally used in the field of vaccines: diphtheria toxoid, tetanus toxoid, nontoxic mutant form CRM_{197} of diphtheria toxoid, outer membrane protein type 1 (OMP1) of ~~Neisseria meningitidis~~*Neisseria meningitidis*, as well as any native or synthetic peptide or polypeptide capable of fulfilling the same function, for example the peptides described in the patent application WO 98/31393.

Please replace the paragraph at page 8, lines 3-11 with the following amended paragraph:

Five groups of 8 female OF 1 mice, weighing 22 to 24 grams, are available. The mice are divided into groups of 8. Each group is used to test one of the vaccine compositions A, B or C obtained in example 1, a vaccine composition serving as negative control (comprising only nonconjugated PRP) and a vaccine composition serving as positive control which consists of the vaccine ~~Act-Hib~~™ACTHIB, which is a Haemophilus b conjugate vaccine (Tetanus toxoid conjugate) marketed by the company PASTEUR MERIEUX Sérum and Vaccins.